

DETAILED OFFICE ACTION

Applicant's response filed 05/02/2011 is acknowledged.

Claims 1-44 are pending. Claims 39-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Further, claims 8-20, 22, 23, and 27-31 are withdrawn from further consideration as being directed to nonelected species of invention. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/05/2010. Claims 1-7, 21, 24-26, and 32-38 are currently under examination.

Withdrawal of Claim Rejections - 35 USC § 101

The rejection of claims 1-7, 21, 24-26, and 32-38 under 35 USC 101 because the claimed invention is directed to non-statutory subject matter is withdrawn in view of amendments made to the instant claims. While all the process steps involved in predicting and calculating and comparing exchange data so as to arrive at a prediction of high resolution protein structure remain silent with regard to a specific tie to any machine or apparatus, applicants have amended the recited 3D structure determination process so as to recite a physical step of "experimentally determining protein amide exchange rates". Since this newly recited data collecting step is a physically transformative step expressly recited in the claim, the examiner has withdrawn the previous grounds of rejection.

Withdrawal of Claim Rejections - 35 USC § 102

The previous rejection of claims 1 and 32-35, 37 and 38 under 35 U.S.C. 102(e)(2) as being by Hilser et al. is withdrawn in view of amendments made to the instant claims and in view of the new grounds of rejection set forth below under 35 USC 112, 1st paragraph.

Withdrawal of Claim Rejections - 35 USC § 103

The previous rejection of claims 1 and 32-38 under 35 U.S.C. 103(a) as being unpatentable over Hilser et al. in view of Simons et al. is withdrawn in view of amendments made to the instant claims and in view of the new grounds of rejection set forth below under 35 USC 112, 1st paragraph.

Response to Arguments

Applicant's arguments filed 05/02/2011 have been considered but are moot in view of the new ground(s) of rejection set forth below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 21, 24-26, and 32-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to use the claimed invention one of skill in the art must be able to determine the three dimensional of a protein of unknown structure based only on amide hydrogen-deuterium exchange mass spectroscopy data. For the reasons discussed below, there would be an unpredictable amount of experimentation required to practice the claimed invention.

b) The specification describes the collection of amide hydrogen-deuterium exchange data on proteins and correlating the observed exchange rates of labile hydrogen to secondary structural (two-dimensional) characteristics. The specification does not describe any procedure by which tertiary structural (three-dimensional) characteristics of a protein can accurately or meaningfully derived from using only labile hydrogen position and observed exchange rates with solvent.

c) The specification does not provide any examples wherein "a protein of interest of unknown structure" had a three-dimensional structure determined using only the hydrogen-deuterium exchange mass spectroscopy data as instantly claimed. It is further emphasized that applicants arguments filed 05/02/2011 emphasize that the claimed invention "is directed to all the determination of structures of proteins of unknown structure" (emphasis in the original, see page 10, line 9-12 of applicant's response filed 05/02/2011). Rather, the only working example proved in the instant specification involved the concurrent use of X-Ray crystallographic data in conjunction with the hydrogen-deuterium exchange mass spectroscopy data.

d) The nature of the invention, determination of three-dimensional protein structure for proteins of unknown structure, is extremely complex.

e) The prior art does not show that meaningful predictions of three dimensional structure proteins of unknown structure can be determined absent extensive empirical investigations involving a plurality of spectroscopic applications. Ginalksi et al. is relied upon for the discussion of protein structure determination protocols and providing a summary of practical lessons for protein structure prediction. It is emphasized therefrom

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that “(t)heoretically, it should be possible to deduce structure from sequence by accurate simulation of physical processes. We are very far from achieving this goal.”

See Ginalski et al., page 1874.

f) The skill of those in the art of protein structure determination is extremely high.

g) The predictability of an arbitrary structure of an unknown protein is not known in the prior art.

h) The claims are broad in that they are drawn to determination of any and all proteins of unknown structure, and determining the structure thereof based only on hydrogen and deuterium exchange rate data alone.

The skilled practitioner would first turn to the instant specification for guidance in using the claimed invention. However, the disclosure lacks clear evidence that meaningful three-dimensional structures can be predicted from only hydrogen exchange rate data for observable labile positions in a protein. As such, the skilled practitioner would turn to the prior art for such guidance, however the prior art does not teach that three dimensional structure can be derived from exchange rate data alone. Finally, said practitioner would turn to trial and error experimentation to determine what, if any, meaningful three-dimensional structures can be derived from exchange rate data alone. Such amounts to undue experimentation.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ERIC S. DEJONG whose telephone number is (571)272-6099. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/ERIC S DEJONG/

Primary Examiner, Art Unit 1631